RESEARCH LETTER

Stroke risk reduction after left atrial appendage occlusion in elderly patients with atrial fibrillation: long-term results

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Introduction In patients with nonvalvular atrial fibrillation (AF), age is a nonmodifiable risk factor for thromboembolism, based on the CHA_2DS_2-VASc score (congestive heart failure, hypertension, age >75 years, diabetes mellitus, history of stroke or thromboembolism, vascular disease, age 65 to 74 years, female sex), and for bleeding, based on the HAS-BLED score (hypertension, abnormal liver function, history of stroke or thromboembolism, history of bleeding, age ≥65 years, use of nonsteroidal anti-inflammatory drugs, and alcohol abuse). Also, the prevalence of AF increases with age, from 0.5% among patients aged 50 to 59 years to 10% among those aged over 80 years. Therefore, nonvalvular AF is one of the most significant causes of embolic stroke in people over 75 years of age.[1]

Left atrial appendage (LAA) occlusion is an alternative treatment for the prevention of stroke and systemic thromboembolism in patients with nonvalvular AF. Previous studies showed that LAA occlusion procedures are efficacious, safe, and widely performed in clinical practice. However, there is concern that elderly patients are more susceptible to complications, and thus the risk of performing LAA occlusion in elderly patients may be too high.

In this study, we present long-term results of stroke and bleeding reduction after LAA occlusion based on the patient's age.

Material and methods A retrospective, single-center study was performed in 139 consecutive patients with nonvalvular AF, who underwent LAA occlusion with the LARIAT device (SentreHEART Inc, Redwood, California, United States). Patients were divided into 3 groups depending on age: <65 years, 65 to 74 years, and ≥75 years.

Postprocedural anticoagulation and optimization of anticoagulant therapy was individualized depending on the patient's history, contraindications, risk of stroke and bleeding, and patient or physician preferences. Transesophageal echocardiography at 30 days after the procedure was performed to monitor for postoperative leak.

Freixa et al[2] reported adverse events during follow-up, based on VARC-2 criteria.[3] In line with the study by Freixa et al,[2] procedure efficacy to prevent thromboembolic events (stroke, transient ischemic attack [TIA], and systemic embolism) was tested by comparing the actual event rate at follow-up with the event rate predicted by the CHA_2DS_2-VASc score.[4] Individual patient annual risks were recorded, and the average annual risk for the whole study population was calculated. The total number of thromboembolic events during the overall follow-up period was divided by the total number of patient-years of follow-up and multiplied by 100 to obtain the actual annual rate of thromboembolism. Thromboembolism rate reduction was calculated as follows: (estimated% – actual% event rate) / estimated% event rate. Bleeding reduction rate was based on the HAS-BLED score and was assessed using the same method as for stroke risk reduction. Differences with a P value of less than 0.05 were considered significant.

Results LAA occlusion was performed in 139 patients. At the time of the procedure, 82 patients were aged 64 years or younger, 44 patients were aged 65 to 74 years, and 13 patients were aged 75 or older (P <0.001). Patients aged 75 years

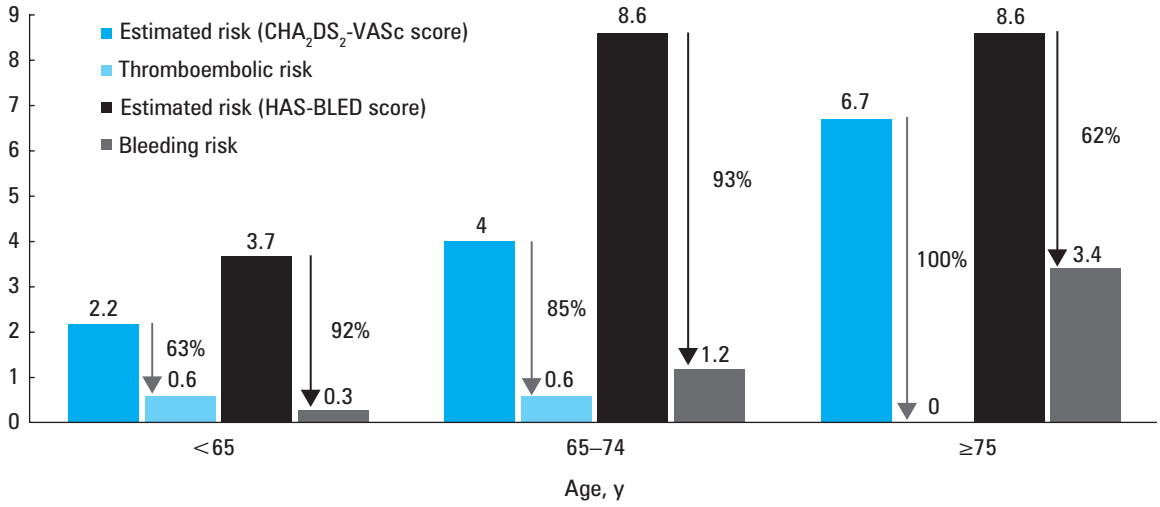

FIGURE 1 Effectiveness of left atrial appendage occlusion in stroke and bleeding risk reduction (100 patient-years) during the overall follow-up in the study groups divided according to age

or older had a higher risk of stroke based on the $CHADS_2$ and CHA_2DS_2-VASc scores (3.2 and 4.8, respectively) compared with patients aged 64 years or younger (1.2 and 1.9, respectively) and those aged 65 to 74 years (2.6 and 4.3, respectively) ($P = 0.001$ and $P = 0.001$, respectively). Patients aged 65 to 74 years had the highest risk of bleeding based on the HAS-BLED score (3.8), as compared with those aged 64 years or younger (2.6) and those aged 75 years or older (3.6) ($P = 0.001$ for all comparisons). Patients aged 65 to 74 years had also the highest proportion of females ($P < 0.001$) and of patients with a previous stroke / TIA ($P = 0.03$). There were no significant differences in other comorbidities, stroke risk factors, antithrombotic treatment, or LAA dimensions. Transesophageal echocardiography performed 30 days postprocedure showed no significant differences in the prevalence of postoperative leak.

One year after the procedure, 12 patients were lost to follow-up. Overall, the follow-up study population was 530.1 patient-years. The overall follow-up of the study population was 50 months in patients aged 64 years or younger, 51 months in those aged 65 to 74 years, and 54.5 months in those aged 75 years or older. There were no differences in antithrombotic treatments after follow-up ($P = 0.25$).

During follow-up, 2 cardiovascular deaths occurred, which were unrelated to the procedure, 2 episodes of serious bleeding, and 1 episode of stroke. There were 2 thrombi in the LAA diagnosed by follow-up echocardiography. These were successfully managed with unfractionated heparin with no further complications. All reported events were included in the analysis of this study.

There were no significant differences between groups with regards to mortality, thromboembolic events (stroke / TIA, systemic embolism), and bleeding. The overall estimated annual risk reduction of thromboembolic events and major bleeding was 81% and 86%, respectively (FIGURE 1).

Discussion Previous studies on LAA occlusion procedure have included patients aged under 75 years, but few examined the safety and efficacy of LAA occlusion in patients older than 75 years.[2,5,6] Compared with previous studies, our results are remarkable for 2 reasons. Firstly, all previous studies presented the results of LAA occlusion using a variety of endocardial devices,[2,6] except Gafoor et al,[5] who used the LARIAT device in only 5% of patients. We are the first to present the results of the LAA occlusion procedure using LARIAT in elderly patients. Secondly, we present the longest follow-up period after LAA occlusion in elderly patients.

Our long-term follow-up results showed a similar reduction in thromboembolic risk after LAA occlusion in all 3 age groups. The results were similar to those reported in previous studies.[2,5,6] Of note, both the $CHADS_2$ and CHA_2DS_2-VASc scores were significantly higher in patients aged 75 years or older, who had no thromboembolic complications. Therefore, based on the estimated thromboembolic risks according to the CHA_2DS_2-VASc score, patients aged 75 years or older present the highest reduction in relative risk for thromboembolism compared with the general population (FIGURE 1). These results correlate with data from the study by Freixa et al.[2]

It should be also noted that incomplete ligation and size of the leak after LAA occlusion with LARIAT had no clinical significance for developing thrombosis or stroke. Two diagnosed thrombi and stroke in our study were found in patients with complete LAA closure with no significant differences in patient age. Similar results were obtained in the LAA occlusion procedure with endocardial devices.[2,7]

The relative bleeding risk reduction was reduced in all 3 groups, which is similar to findings from previous studies.[2,5,6] As expected, the lowest reduction was observed in patients aged 75 years or older (FIGURE 1). Importantly, there were no significant differences in antithrombotic treatments

after follow-up. The study by Freixa et al[2] showed no significant differences in bleeding rates among patients aged 75 years or older and those younger than 75 years despite higher HAS-BLED scores in the older group. In our study, there were no significant differences in bleeding rates; however, the bleeding rate in patients aged 75 years or older was higher in our study than that reported by Freixa et al[2] (8.3% and 2.3%, respectively).

Several mechanisms significantly increase the risk of bleeding in elderly patients.[4] The greatest benefits from oral anticoagulation (OAC) are observed in elderly and high-risk patients, although OAC also increases the risk of serious bleeding with age.[4,8] Optimal international normalized ratio control in elderly patients is difficult to achieve, and almost 50% of older patients do not reach a therapeutic range. In contrast to vitamin K antagonists, non–vitamin K antagonist oral anticoagulants are reported to have a shorter half-life; moreover, they slightly reduce the risk of hemorrhagic bleeding but are not free from complications.[9] Of note, more than 20% of patients with nonvalvular AF receive inappropriate antithrombotic therapy.[10] Elderly patients also have a higher frequency of comorbidities that increase the risk of bleeding, such as hypertension, liver failure, renal insufficiency, anemia, malignancy, or coronary artery disease with concomitant antiplatelet therapy.[4] In our study, all bleeding events were intracranial; 3 patients were on anticoagulation therapy and 1 event was due to uncontrolled hypertension.

In our previous study, we showed that LAA occlusion with LARIAT is a safe procedure with high success rates.[11,12] Long-term follow-up shows no differences in mortality due to cardiovascular and noncardiovascular causes. Our results correlate with data from other studies[2,6]; however, the mortality rate in our group was lower compared with that reported by Davtyan et al.[6] Due to natural outcomes, mortality rate in patients aged 75 years or older was higher compared with the other age groups, but this difference was not significant. Thus, overall the LAA occlusion procedure has no effect on mortality regardless of patient age.

Study limitations This was a nonrandomized, retrospective, observational study of procedures performed by one experienced operator. The major limitation for estimating the overall value of LAA occlusion is the lack of a control group and only a calculated stroke or bleeding risk. Also, 12 patients were lost to follow-up after 1 year (8.6%). Another limitation were unequally sized groups. Long-term results for thromboembolic event reduction are confounded by the high proportion of patients on OAC at the time of their last follow-up visit. Several antithrombotic drugs with different pharmacological properties and indications were prescribed; however, there were no significant differences between the groups.

Conclusions Our results suggest that LAA occlusion with LARIAT has a similar safety endpoint and long-term efficacy in elderly patients as LAA occlusion in the general population. Moreover, it is associated with similar stroke and bleeding rates, as well as similar mortality rates, regardless of age. Finally, estimated thromboembolic and bleeding risk reductions were observed in all 3 age groups.

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